REMARKS

Applicants respectfully request that this application be reconsidered in view of the above amendments and the following remarks.

1. Status of the Claims

Claims 1-31 are currently pending in this application for examination on the merits.

2. <u>Summary of the Amendments</u>

Claim 2 has been rewritten in independent form and now recites that the glycopeptide "comprises a carboxy-terminus". Additionally, the term "C-terminus" has been rewritten as "carboxy-terminus". Support for these amendments is found, for example, on page 3, lines 14-19; page 30, lines 08-10; and in original Claim 2.

Similarly, Claim 3 has been rewritten in independent form and now recites that the glycopeptide "comprises a 1,3-dihydroxyphenyl moiety". Additionally, the term "R-position" has been rewritten as the "2-position of the 1,3-dihydroxyphenyl moiety". Support for these amendments is found, for example, on page 3, line 23 to page 4, line 01; page 34, lines 16-18; formula I at page 4, line 13; formula II at page 16, line 01; and in original Claim 3.

Claim 4 has been amended to delete the phrase "at the R-position", since this phrase is redundant and therefore unnecessary, given the dependency of Claim 4 on Claim 3.

Claim 5 has been rewritten in independent form. Additionally, the word "to" has been added before "form a heterocyclic ring" at page 83, lines 03 and 13 to correct an obvious and inadvertent typographical error.

Claim 13 has been amended to correct an obvious typographical error, i.e., the -CH-group has been corrected to a -CH₂- group. Support for this amendment is found on page 13, line 22 to page 14, line 01; and in Claim 12 as originally filed.

Claim 19 has been amended to delete a bracket, i.e., "[" in the chemical formula at page 88, line 17, and replace it with a parenthesis, i.e., "(", to correct an obvious and inadvertent typographical error.

Claim 28 has been amended to make it dependent on Claim 2 instead of Claim 1.

Additionally, the term "C-terminus" has been replaced with "carboxy-terminus".

Similarly, Claim 29 has been amended to make it dependent on Claim 3 instead of Claim 1. Additionally, the term "R-terminus" has been replaced with "2-position of the 1,3-dihydroxyphenyl moiety".

Claim 31 has been amended to replace the phrase "any one of claims 23" with "claim 23" to correct an obvious and inadvertent typographical error.

Pursuant to 37 C.F.R. §1.121, a marked-up version showing the changes made to the claims is attached. The above amendments are being made for cosmetic reasons and are not believed to change the scope of the amended claims in any way. No new matter is introduced by these amendments. Accordingly, entry of these amendments is respectfully requested.

3. Rejection Under 35 U.S.C. §112, Second Paragraph

Claims 3, 4, 29 and 31 have been rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as their invention. Specifically, the Examiner has indicated that there is no antecedent basis for the phrase "the R-terminus" in Claims 3, 4 and 29.

In response, Applicants have amended Claim 3 to recite that the glycopeptide comprises a 1,3-dihydroxyphenyl moiety (i.e. a resorcinol-like moiety) and that the 2-position of the 1,3-dihydroxyphenyl moiety (i.e., the position between the hydroxy groups) is substituted with the phosphono-containing substituent. Additionally, the term "R-terminus" has been deleted from Claim 4; and replaced in Claim 29 with the term "2-position of the 1,3-dihydroxyphenyl moiety". Accordingly, Applicants respectfully request that the rejection of Claims 3, 4, and 29 under 35 U.S.C. §112, second paragraph, be withdrawn.

Additionally, the Examiner has indicated that "some part of the dependency is missing" from Claim 31. In response, Applicants have corrected a typographical error in Claim 31 by replacing "any one of claims 23" with simply "claim 23". Thus, the rejection of this claim under 35 U.S.C. §112, second paragraph, may be withdrawn.

4. Objections

Claims 5-7, 19, 23-27, 30 and 31 have been objected to due to informalities.

Specifically, the Examiner has indicated that Claim 5 should be amended at page 83, lines 03 and 13, to insert "to" before "form". In response, Applicants have amended Claim 5 as suggested by the Examiner.

Additionally, the Examiner has indicated that, in one of the chemical formulas of Claim 19, the beginning bracket does not match the end parenthesis. In response, Applicants have corrected this typographical error.

Accordingly, Applicants respectfully requested that the objection to Claims 5-7, 19, 23-27, 30 and 31 be withdrawn.

5. Rejections Under 35 U.S.C. §102(a)

Claims 5-8, 10, 23, 30 and 31 have been rejected under 35 U.S.C. §102(a) as being anticipated by International Publication No. WO 00/39156, published on July 6, 2000. Specifically, the Examiner has indicated that WO 00/39156 teaches Compound 144 at pages 19 and 30, "which compound comprises a phosphonate [sic] group at a position corresponding to Applicants' R³ substituent."

Similarly, Claims 1, 2, 5-8, 10, 14, 16, 19, 23, 28, 30 and 31 have been rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,392,012, issued to Judice et al. U.S. Patent No. 6,392,012, which is the U.S. equivalent of WO 00/39156, discloses Compound 144 in Columns 15-16 and the Examiner has indicated that the specified claims are anticipated for the same reasons given for WO 00/39156.

For the following reasons, Applicants respectfully disagree with the assertion that the specified claims are anticipated by the cited references.

Anticipation under 35 U.S.C.§102 requires that each and every element of the claimed invention be disclosed in a prior art reference. A reference that merely discloses similar but not identical elements is insufficient to anticipate the claimed invention.

In the present case, WO 00/39156 and U.S. Patent No. 6,392,012 disclose (as Compound 144) a vancomycin derivative having, among other substitution, a phosphate-containing group of the following formula at the carboxy-terminus:

i.e., an *N*-[2-amino-2-deoxy-6-(dihydrogen phosphate)glucopyranose. Thus, Compound 144 differs from Applicants' presently claimed invention in that Compound 144 contains a phosphate group (i.e., -O-P(O)(OH)₂) and not a phosphono group (i.e., -P(O)(OH)₂). Using conventional nomenclature for phosphorous-containing compounds, a phosphate group cannot be consider to comprise a phosphono group because the additional oxygen atom of the phosphate makes it a derivative of phosphoric acid (i.e., P(O)(OH)₃) not phosphonic acid (i.e. HP(O)(OH)₂).

Therefore, since the glycopeptide compound disclosed in WO 00/39156 does not contain a phosphono group, this reference cannot anticipate Applicants' presently claimed invention. Accordingly, Applicants respectfully request that the rejection of Claims 5-8, 10, 23, 30 and 31 under 35 U.S.C. §102(a), and the rejection of Claims 1, 2, 5-8, 10, 14, 16, 19, 23, 28, 30 and 31 under 35 U.S.C. §102(e) be withdrawn.

6. Rejections Under 35 U.S.C. §103(a)

Claims 24-27 have been rejected under 35 U.S.C. §103(a) as being obvious over International Publication No. WO 00/39156, published on July 6, 2000, in view of U.S. Patent No. 4,983,586, issued to Bodor. Similarly, Claims 24-27 have been rejected under 35 U.S.C. §103(a) as being obvious over U.S. Patent No. 6,392,012, issued to Judice, in view of

U.S. Patent No. 4,983,586, issued to Bodor. For the following reasons, Applicants respectfully disagree with the conclusion that the specified claims are obvious in view of the cited references.

To establish a *prima facie* case of obviousness, the Examiner must make three showings. First, the Examiner must show that the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, contained some suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine references in a manner that produces the claimed invention. Second, the Examiner must show that the proposed modification of the prior art references had a reasonable expectation of success as determined from the vantage point of one of ordinary skill in the art. And lastly, the Examiner must show that the prior art reference or combination of references teach or suggest all the limitations of the claims.

In the present case, Claims 24-27 are directed to a pharmaceutical composition comprising a pharmaceutically-acceptable carrier; a glycopeptide substituted with one or more substituents each comprising one or more phosphono groups; and a cyclodextrin.

The Examiner has indicated that Claims 24-27 are obvious over U.S. Patent No. 6,392,012 or WO 00/39156 in view of the Bodor reference because:

[i]t would have been obvious to one of ordinary skill in the art...to include the hydroxypropyl- β -cyclodextrin of Bodor in the aqueous solutions of the compound of the WO Patent Application '156 because the hydroxypropyl- β -cyclodextrin would have been expected to improve the solubility and/or stability of the compound of the WO Patent Application '156. Office Action at Pages 4-5.

However, as discussed above, the phosphate compound disclosed in U.S. Patent No. 6,392,012 and WO 00/39156 is not encompassed within the scope of Applicants' claimed subject matter. Accordingly, even if one skilled in the art combined the disclosed phosphate compound with the teachings of Bodor, the skilled artisan would not produce the subject matter of Applicants' Claims 24-27. Moreover, the cited references fail to provide any motivation to one skilled in the art to modify their teachings in a manner that produces the

subject matter of Claims 24-27.

Therefore, since the cited references do not teach or suggest all the limitations of Applicants' claimed subject matter nor do they provide the requisite motivation to produce the claimed subject matter, Applicants respectfully submit that these references do not establish a prima facie case of obviousness. Accordingly, Applicants respectfully request that the rejection of Claims 24-27 under 35 U.S.C. §103(a) be withdrawn.

7. Allowable Subject Matter

Applicants note with appreciation that the Examiner has indicated that Claims 9, 11-13, 15, 17, 18 and 20-22 would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Additionally, Claims 3, 4 and 29 have been indicated to be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. §112, second paragraph and to include all of the limitations of the base claim and any intervening claims.

For the foregoing reasons, Applicants believe that this application is now in condition for allowance and a notice to that effect is respectfully requested. Should there be any remaining issues that can be resolved by telephone, the Examiner is respectfully requested to telephone the undersigned attorney at (650) 808-6406.

Respectfully submitted,

THERAVANCE, INC.

Date: January <u>15</u>, 2003

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